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Online monitoring in continuous renal replacement therapies

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Online monitoring in continuous renal replacement therapies. Technical improvements in dialysis equipment for chronic hemodialysis patients has mirrored improvements in continuous renal replacement therapies (CRRTs) for patients with acute renal failure who are critically ill. This article reviews the available types and importance of online monitors such as urea sensors to provide real-time urea kinetic parameters, temperature sensors to target thermal balance throughout each session, conductivity measurement of sodium balance in the dialysate, blood volume monitoring to aid against cardiovascular instability and treatment-induced hypotension, biofeedback systems, and remote dialysis/teledialysis for efficient use of trained personnel.

Continuous renal replacement therapies (CRRTs) are today considered a well-tolerated and efficient group of treatments for acute renal failure in critically ill patients [1–3]. The evolution in technology of CRRT has only partially followed the more sophisticated evolution that took place in the equipment for chronic hemodialysis patients [4–10]. In such patients, the increased morbidity and the progressively increased age require a gentle and carefully monitored hemodialysis therapy [11–20]. To achieve such results, online monitoring of patient and machine parameters may become an important issue, although it includes some practical considerations (Table 1). Different parameters could be monitored according to the technical and clinical requirements (Table 2). Based on the available technology, some techniques for online monitoring in dialysis have been developed, including urea sensors, temperature sensors, blood volume sensors, and teledialysis or biofeedback systems. This review attempts to analyze how this new technology could have a positive impact in acute patients and how it could be implemented in the present equipment for CRRT.

ONLINE UREA MONITORING

There are several urea sensors available on the market that are generally integrated in the hemodialysis machines for chronic patients (Table 3). The scope of this technology is to achieve information in real time on the efficiency of the system and on the urea kinetic parameters relevant to the dialysis session (abstract; Keshaviah et al, *J Am Soc Nephrol* 3:374, 1992; abstract; Depner et al, *J Am Soc Nephrol* 4:343, 1993) [21–35]. The technology is based on the analysis of the spent dialysate leaving the dialyzer (Baxter Biostat 1000; Gambro UQM, Hospal Diascan, UM Fresenius, Bad Homburg, Germany) or of the ultrafiltrate produced in a hemofiltration unit (UMS Bellco, Mirandola, Italy). All of these sensors use the enzymatic reaction promoted by urease that leads to formation from urea molecules of ionic species that can be measured in a conductivity cell [36]. Because the same measurement is done on the fluid before the passage through the enzyme, the differential conductivity measurement can provide information on the amount of urea removed. All of these monitors offer a series of calculations of urea kinetic parameters, and they are also capable of presenting a predicted result for the session. In this way, the operator can modify the operational parameter to achieve the desired results.

This technology has not been used for CRRT machines, and it has not been applied to acute patients treated with continuous therapies. The slow progressive removal of solutes in CRRT permit an equilibrium between removal and generation to be reached, so that constant blood levels can be observed at a steady state. Under these circumstances, the need for online measurement of urea kinetic parameters is not required, and daily or twice daily blood chemistry measurements should be sufficient to describe and monitor treatment efficiency. Therefore, the use of online monitors for urea or other solutes in these patients may not represent a significant advantage, and we do not foresee the use of urea sensors in CRRT, at least in this generation of machines [37].

ONLINE TEMPERATURE SENSORS

This technology has mostly been proposed by Fresenius as part of the latest generation of dialysis machines for chronic patients. The technology consists of the placement

Key words: acute renal failure, critical care monitoring, urea kinetics, blood chemistry.

Table 1. Aspects of on-line monitoring in CRRT

•Invasivity
• Frequency of measurement
• Accuracy of measurement
• Technology involvement
• Cost of the required hardware
• Cost of the required disposable
• Cost of the software
• Significance of the monitored parameter

Table 2. Parameters that could be monitored on-line

Patient	Treatment
• Arterial blood pressure and O_2	• Blood and dialysate flow rates
• Heart rate and ECG	• Extracorporeal circuit pressures
• Hydration and nutrition	• Access condition and recirculation
• Whole body clearances (urea)	• Efficiency (dialysance, Kt/V)
• Blood volume changes	• Ultrafiltration rate and control
• Electrolytes and acid-base	• Effective delivery (blood processed)
• Energy and thermal balance	• Dialysate quality (HFD-OLHDF)
• Bioincompatibility reactions	• Dialysate composition and temperature

Table 3. On-line urea monitoring systems

Name	Company	System
Biostat 1000	Baxter	Repeated measurements of spent dialysate
UMS	Bellco	Continuous measure of blood ultrafiltrate
DQM	Gambro	Continuous measure of dialysate spill off
Diascan	Hospal	Based on ionic dialysance
Urea module	Fresenius	Based on ionic dialysance

of isolated temperature sensors on the arterial and venous line of the extracorporeal circulation. This equipment not only allows for the calculation of the thermal balance in a single session, but it also permits achievement of a target value of body temperature in the patient at the end of the session (Fig. 1). This is obtained by a controlled variation in the temperature of the dialysis solution. The possibility of delivering a thermal bolus by injection of cold saline in the venous line or by a sudden decrease in the temperature of dialysate allows for the measurement of the recirculation in the vascular access. This feature of the blood temperature monitor (BTM) would be of great interest for the acute patient, since the critically ill patient may frequently be hyperthermic, and he or she may require a progressive cooling to improve hemodynamic stability and to prevent thermal damage. On the other hand, when large volumes of fluid are exchanged in hemofiltration, the risk of a negative thermal balance is greatly enhanced. For all of these aspects, the use of BTM in the acute patient should be probably encouraged, and future application of these monitors in CRRT machines is highly recommended [38].

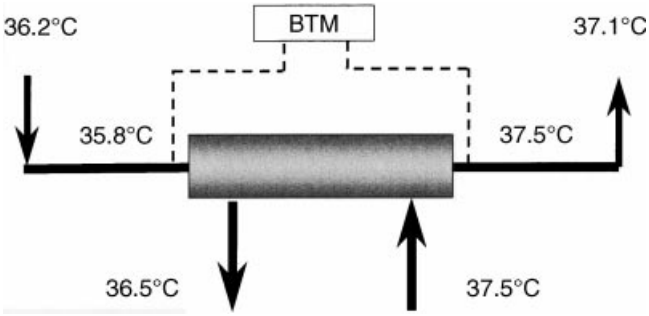

Fig. 1. Typical thermal energy balance in hemodialysis. The blood temperature monitor (BTM) consists of two sensors placed on the arterial and venous line of the extracorporeal circulation.

ONLINE CONDUCTIVITY MEASUREMENT

The use of conductivity cells on the inlet and outlet dialysate lines has been proposed not only to achieve ionic dialysance and therefore to monitor treatment efficiency, but also to provide accurate information on sodium balance. This could only be seen as passive and retrospective information. However, in a system in which the sodium concentration of inlet dialysate (or replacement solution) could be varied manually or automatically, this may represent a tool to target the final sodium balance or to set a predetermined sodium concentration that should be reached by the patient at the end of the session. Thanks to detailed information collected by such a system, modifications in the composition of dialysate or replacement solution may be actuated in order to correct electrolyte imbalances, vascular tone and reactivity, extracellular fluid volume, and composition. This, however, would require an online preparation of the solutions for dialysate or replacement from treated water and concentrated salts. This technology is on its way, and has already been applied in the chronic patient. Future developments may likely include the application of this technology to the critically ill patient.

BLOOD VOLUME MONITORING

Cardiovascular instability, hypotension, and shock represent a frequent complication of extracorporeal renal replacement therapies. Such events have been correlated with the rate of ultrafiltration obtained during therapy. In particular, when the ultrafiltration rate exceeds 0.25 ml/min/kg, the chance of hypotensive episodes increases exponentially [5]. The pathophysiological foundations of this complication are based on a discrepancy between the speed of fluid extraction by the artificial membrane and the rate of intravascular refilling from the interstitial and intracellular space. Such a refilling is dependent on myocardiac function, vascular permeability, and oncotic power of plasma in the presence of an intact endothelial barrier. Because such a discrepancy

results in significant circulating blood volume variations, online monitors have been designed to evaluate relative blood volume changes during extracorporeal treatments and to obtain directions for intravenous infusions in real time. These monitors are based on different methods, but they are all characterized by the capability of obtaining an accurate measurement of relative blood volume variations. Because red blood cell mass and hemoglobin cannot change during treatment, relative changes in the concentration of hemoglobin or hematocrit must be related to a variation of blood water content. As a consequence, variations of circulating blood volume can be derived in a percentage.

Cardiovascular instability and treatment-induced hypotension may be even more frequent in critically ill patients with acute renal failure. To prevent vascular instability and dialysis-induced hypotension, CRRTs, instead of daily intermittent hemodialysis (DIHD), have been used in such patients. Improved clinical tolerance is ensured because of a slow continuous ultrafiltration over an extended period of time. For example, assuming a fluid input of 4000 ml/24 hr in a completely anuric patient in the intensive care unit (ICU), the ultrafiltration rate required to restore an adequate fluid balance would be of one order of magnitude less in CRRT than in a daily four-hour hemodialysis session (2.7 ml/min in CRRT vs. 16.6 ml/min in DIHD). Therefore, in CRRT, intravascular refilling may likely take place at a speed that is adequate in preventing significant variations of circulating blood volume. Blood volume monitors have been used in the critically ill patients by our group.

We carried out a prospective randomized cross-over study on 10 patients with acute renal failure treated in a random sequence with a 4-hour hemodialysis session (DIHD) and a 24-hour continuous venovenous hemofiltration (CVVH) session. In all cases, a special device (Crit-Line; In-line Diagnostics, Salt Lake City, UT, USA) was used to detect online blood volume changes and to correlate these changes with the patient's hemodynamic response. Patients were admitted to the nephrology ward and/or ICU. Acute renal failure originated from different causes (6 postsurgical and 4 toxic nephropathy). During treatment, careful attention was paid to prevent variations in body temperature and baseline vasopressor pharmacological treatment. The intermittent hemodialysis session was performed for four hours with a blood flow of 250 ml/min, using an AN69 dialyzer of 1.3 m^2. The dialysate flow rate was 500 ml/min, and the dialysate sodium content was 140 mEq/liter. Once established, the desired weight loss time was scheduled on the basis of a maximum ultrafiltration criterion. Ultrafiltration was set to not exceed 0.24 ml/min/kg body wt (approximately 1 liter/hr in a 70 kg patient). Bicarbonate was used as a buffer in dialysis fluid. The CVVH session was performed with an AN69 hollow fiber hemofilter 0.6 m^2, with a blood flow of 200 ml/min for a total of 24 hours. A total of 48 liters of ultrafiltrate was produced with an average ultrafiltration rate of 2 liter/hr. The replacement solution contained 140 mEq/liter of sodium and bicarbonate as a buffer. The net ultrafiltration was scheduled according to the weight loss requirements.

Hydration status was stabilized before the study, and in both treatments, the patients required an average volume of ultrafiltration of approximately 3 liter/24 hr.

Both treatments were monitored with a continuous arterial blood pressure recording (radial artery) and continuous blood volume measurement (Fig. 2). The monitor is characterized by two components: the sensor and the display unit. The sensor is in the form of a clip that is applied to the prefilter line of the extracorporeal circulation. A special disposable transparent cell is connected to the line before the hemodialyzer, and the sensor clip is placed exactly on this cell. The sensor operates by sending a light beam across the transparent cell inside which blood is flowing. Because of the defined frequency of the light beam and the red cells' tendency to reflect the light, the sensor clip can detect even minimal scattered variations caused by changes in the hematocrit concentration. The sensor is then connected by a cable to the monitor that reports blood volume changes in real time on a graphic display. The method has been previously validated, and it permits detection of even slight variations in hematocrit reflecting parallel variations in circulating blood volume. It should be noted that other BVMs are available on the market, but most of them are part of a chronic dialysis machine and are not a self-standing unit. For this reason, we selected the Crit-Line in order to apply the monitor to our CRRT machines manufactured by different companies.

Table 4 reports the metabolic data and clinical parameters recorded before and after the different treatments.

Due to the intermittent nature of DIHD, the results achieved refer to an average treatment time of 230 $\pm$ 15 minutes. In contrast, the CVVH results refer to a mean treatment duration of 1400 $\pm$ 80 minutes. As a consequence, wide shifts in biochemistry profiles are seen in DIHD compared with the more steady conditions recorded in CVVH.

As reported in Figure 3, a significantly higher blood pressure drop is observed during the intermittent hemodialysis session in all patients. The difference in maximal pressure drop is remarkable and statistically significant ($P < 0.001$). The same difference is observed when relative blood volume changes are considered. Greater variations are observed in DIHD compared with a fairly stable behavior of the blood volume during CVVH ($P < 0.001$; Fig. 4).

In Figure 5, we report a typical example of a 48-hour study in 1 of the 10 studied patients. It can be seen that hemodynamic instability is only observed during DIHD,

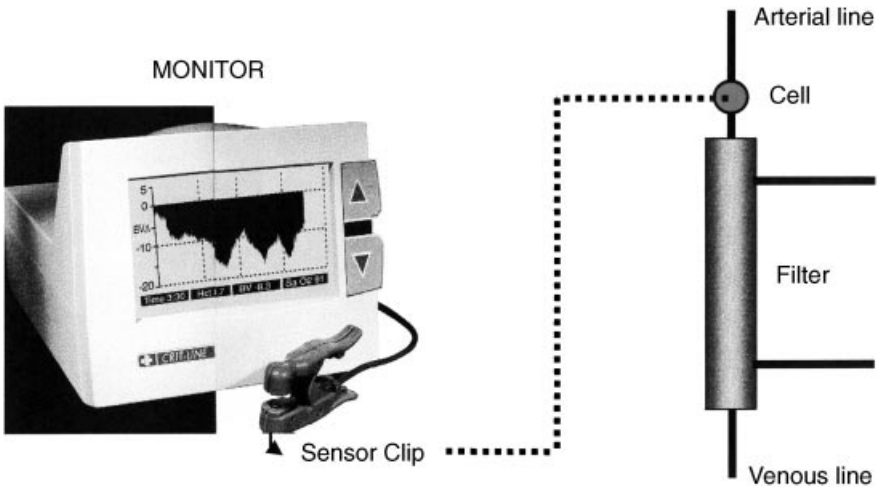

Fig. 2. Schematic representation of a typical online blood volume monitor (Crit-Line; Inline Diagnostics).

Table 4. Treatment parameters

	DIHD	CVVH
Total ultrafiltration	2780 ± 220	2910 ± 330
Ultrafiltration rate *ml/min/kg*	0.19 ± 0.3	0.026 ± 0.03
Blood flow rate *ml/min*	250 ± 15	200 ± 30
Treatment duration *min*	230 ± 15	1400 ± 80
Biochemical and clinical parameters		
	Pre-DIHD	Post-DIHD	Pre-CVVH	Post-CVVH
Urea *mg/dl*	76.5 ± 8.1	26.4 ± 6.3	71.5 ± 3.9	58.2 ± 7.2
Creatinine *mg/dl*	8.3 ± 2.6	3.2 ± 1.4	7.8 ± 1.7	6.3 ± 1.3
Sodium *mEq/liter*	137 ± 3	139 ± 4	137 ± 3	139 ± 2
Potassium *mEq/liter*	5.2 ± 0.4	3.5 ± 0.6	4.9 ± 0.2	4.3 ± 0.2
Chloride *mEq/liter*	5.2 ± 4	100 ± 3	99 ± 6	103 ± 4
Bicarbonate *mmol/liter*	19.3 ± 3	26.9 ± 2	20.1 ± 2	24.9 ± 2
Calcium *mg/dl*	8.9 ± 0.4	10.6 ± 0.6	9.0 ± 0.2	9.7 ± 0.5
Phosphate *mg/dl*	6.8 ± 0.9	3.6 ± 0.5	5.1 ± 0.4	3.6 ± 0.6
Osmolality *mOsm/kg* H_2O	339 ± 10	285 ± 10	334 ± 12	320 ± 13
Mean arterial pressure *mm Hg*	91 ± 13	79 ± 8	90 ± 12	92 ± 10

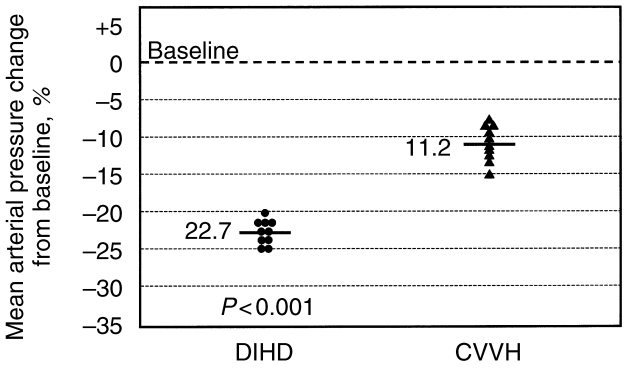

Fig. 3. Peak of mean arterial pressure variation during the two different treatment schedules. The mean arterial pressure reduction is significantly greater in intermittent daily hemodialysis.

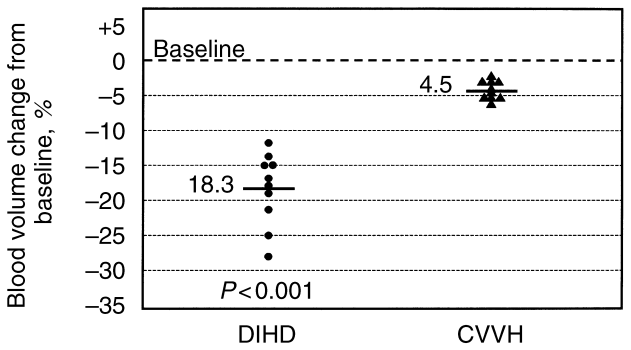

Fig. 4. Peak of relative blood volume change during the two different treatment schedules. Blood volume changes reduction is significantly greater in intermittent daily hemodialysis.

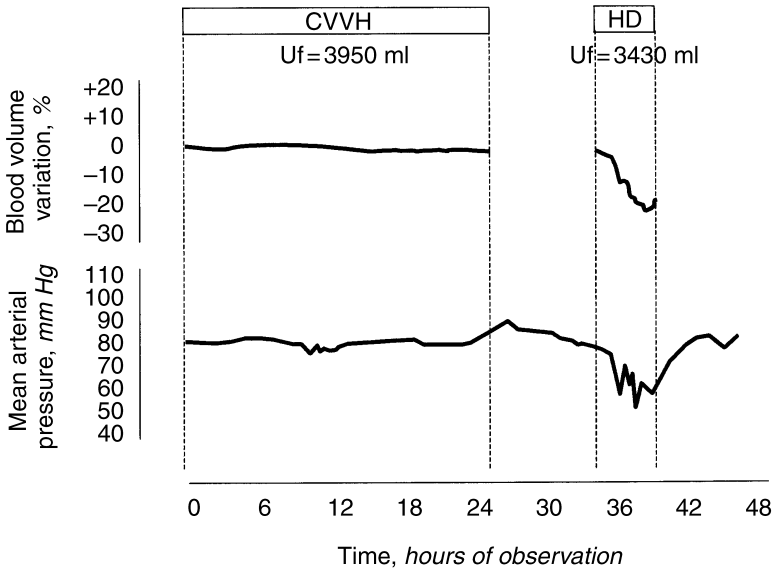

Fig. 5. Typical example of hemodynamic and blood volume monitoring in one of the studied patients. The patient starts on CVVH and is shifted to DIHD on the next day. The reduction in circulating blood volume and blood pressure is remarkable during the intermittent treatment.

and this is directly correlated with a significant decrease in circulating blood volume. In most cases, saline infusion or plasma expander administration was required during DIHD, whereas no variation in substitution fluid administration rate was required during CVVH.

Therefore, it seems that an accurate control of relative blood volume changes may play a pivotal role in the patient's clinical tolerance to the treatment. Among the different parameters, blood volume changes seem to be one of the most important to be monitored in real time. Not only could it suggest a discrepancy between ultrafiltration and refilling, but it could also be applied to obtain information on patient's hydration that is more complete than those offered by noninvasive hemodynamic parameters and/or Swan-Gantz catheters.

TELEDIALYSIS AND REMOTE DIALYSIS CONTROL

In several hospitals, the hemodialysis center is physically located at a distance from the ICU. Under these circumstances, it may become difficult to perform a 24-hour renal replacement therapy. Dialysis nurses cannot follow the patient on a continuous basis and, on the other hand, ICU nurses are not always sufficiently trained to perform the treatment completely. In spite of recent advances in CRRT machines, in which large screens and friendly user interface have been created to make the nurse self-confident with the machine, the troubleshooting procedure suggested by the software is not always adequate to solve the problem at the patient's bedside.

We feel that an important step forward could be played by a cable or modem-connected monitoring system that permits the remote evaluation of alarms and their corrections. Using these systems, which of course require a specific software and an adequate hardware, the treatment carried out in the ICU could be followed and controlled from the dialysis center, thus reducing the burden of sending dialysis nurses over to the ICU at any blinking alarm or the need for substitution fluid bag change.

BIOFEEDBACK SYSTEMS

Today, the availability of online signals from the patient and from the CRRT machine allows an accurate monitoring of the treatment and an adequate correction of clinical and technical problems. This, however, occurs after a careful evaluation of the parameters obtained, a decision-making process that involves some latency, and finally, the action carried out by the personnel to correct the problem. Newer systems have been used in the chronic patient in an attempt to prevent the occurrence of the problem [39, 40]. As an example, the online blood volume measurement joined with a continuous measurement of the arterial pressure can be integrated in a multi-input–multi-output controller that reacts in real time by modifying the rate of ultrafiltration or the conductivity of the dialysis solution. By setting a weight-loss target over time, that is, a profile of allowed blood volume change and other dialysis parameters, it is possible to achieve an automatically controlled dialysis session in which the maximal tolerance is ensured by the controller. This actuates a real biofeedback loop in which not only the latency of the action is reduced or eliminated, but in some cases, the problem is corrected before it becomes clinically significant. This approach that until now has been experimentally used in the chronic patient could

become an important tool for the acute critically ill patient undergoing CRRT.

DISCUSSION

Cardiovascular instability is by far the most common complication during extracorporeal renal replacement therapies. This complication is even more evident in critically ill patients affected by complicated forms of acute renal failure. Because the initial renal insult generally presents a condition of medullary ischemia as the common denominator, any condition that may induce further reduction to the perfusion of the kidney should be strongly prevented. In acute renal failure, the loss of autoregulation is one of the most important pathophysiological alterations affecting the kidney. In the absence of an effective autoregulation, any fall in blood pressure may result in a decreased renal perfusion and in a further ischemic insult. It has been claimed that intermittent hemodialysis may cause severe cardiovascular instability in critically ill patients. According to the mechanism mentioned earlier in this article, intermittent hemodialysis might therefore become a risky procedure in patients with dysfunctioning kidneys, and it may cause further ischemic lesions to the renal parenchyma. In our study, we could confirm that because of the intermittent nature of treatment and the higher rate of ultrafiltration necessary to maintain the patient's fluid balance, remarkable variations in mean arterial pressure are observed during four-hour daily sessions of hemodialysis. This is directly correlated to the variation in the circulating blood volume and therefore to the inability of the patient to experience an adequate intravascular refilling. These alterations are not observed during CRRTs because of the slow continuous nature of the therapy. From these data, it clearly emerges that CRRTs are more adequate to achieve a stable body fluid balance in the critically ill patient. The status of hydration can also be maintained without major variations. In contrast, during DIHD, wide variations of the hydration status are observed because of the intermittent nature of the treatment. Higher ultrafiltration rates are then required to bring the patient to the dry status in a short period of time, and this is obtained at the expense of severe cardiovascular instability. In some cases, it may even become difficult to achieve the desired dry body weight because hypotensive episodes during treatment require the infusion of intravenous fluids or plasma expanders. In this setting, blood volume monitors might be helpful to detect dangerous variations in circulating blood volume. The technology is rather simple, and it can be used in conjunction with any extracorporeal blood therapy. In conclusion, we suggest that blood volume measurement may be a useful tool in preventing major complications during extracorporeal therapies. The possibility of online monitoring such parameters is given by the newly emerging technology. The accuracy of such measurement appears to be enhanced, and this tool may become an important accessory when performing renal replacement therapies in the critically ill patient. Other online monitoring tools, although of some value in the chronic patient, may not be of critical importance for the acute patient undergoing CRRT. Because of the continuous, long-lasting nature of CRRT, rapid variations of other important parameters are not likely to occur. Among the various monitoring systems, the BTM and the teledialysis approaches seem to present some positive aspects and some appealing features. The cost/benefit ratio of such devices has yet to be understood.

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